UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND
TOXIC SUBSTANCES

05/SEPTEMBER/2002

MEMORANDUM

Subject:	Name of Pesticide Product:	Secure Miticide
	EPA Reg. No. /File Symbol:	59639-REG
	DP Barcode:	D283724
	Case No:	071629
	PC Code:	107091
From:	Rick J. Whiting, Biologist	RJW
	Technical Review Branch	
	Registration Division (7505C)	JCR
To:	Geri McCann, PM Team 04	
	Insecticide-Rodenticide Branch	
	Registration Division (7505C)	
Applicant:	Valent U.S.A. Corporation	
	1333 N. California Blvd., Suite 600	
	Walnut Creek, CA 94596-8025	

FORMULATION FROM LABEL:

	Active Ingredient(s):	% by wt.
107091	Etoxazole	72.0
	Inert Ingredient(s):	28.0
	Total:	100.0%

ACTION REQUESTED: PM requests review of acute toxicity data for Secure Miticide, EPA File Symbol 59639-REG.

BACKGROUND: Valent U.S.A. Corporation has submitted a six pack of acute toxicity studies in support of registration of Secure Miticide, EPA File Symbol 59639-REG. The studies were assigned MRID numbers 456216-17 to -22. The studies were conducted at Springborn Laboratories, Inc., Spencerville, Ohio. The product is referred to as "V-1283 72 WDG" in the study reports.

RECOMMENDATIONS: The six studies have been reviewed and are classified as acceptable. The acute toxicity profile for Secure Miticide, EPA File Symbol 1021-REG, is as follows:

Acute oral toxicity	IV	Acceptable	MRID 45621617
Acute dermal toxicity	IV	Acceptable	MRID 45621618
Acute inhalation toxicity	IV	Acceptable	MRID 45621619
Primary eye irritation	III	Acceptable	MRID 45621620
Primary skin irritation	IV	Acceptable	MRID 45621621
Dermal sensitization	Negative	Acceptable	MRID 45621622

LABELING: Based on the toxicity profile above, the following are the precautionary and first aid statements for this product as obtained from the Label Review System.

PRODUCT ID #: 059639-00123

PRODUCT NAME: Secure Miticide

PRECAUTIONARY STATEMENTS

SIGNAL WORD: CAUTION

Hazards to Humans and Domestic Animals:

Causes moderate eye irritation. Avoid contact with eyes or clothing. Wear: Long-sleeved shirt and long pants, socks and shoes.

User Safety Recommendations:

Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco.

First Aid:

If in eyes: Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing. Call a poison control center or doctor for treatment advice.

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-xxx-xxxx for emergency medical treatment information.

DATA EVALUATION RECORD

STUDY TYPE: ACUTE ORAL TOXICITY TESTING (870.1100 formerly §81-1)

Product Manager: 04 **Reviewer:** Rick J. Whiting

TEST MATERIAL PURITY: V-1283 72 WDG; 72% Etoxazole

CITATION: Rodabaugh, D. (2001) An acute oral toxicity in rats with V-1283 72 WDG. Springborn Laboratories, Inc., Spencerville, Ohio. Laboratory Report Number 3548.15. August 13, 2001. MRID 45621617. Unpublished.

SPONSOR: Valent U.S.A. Corporation, 1333 N. California Blvd., Suite 600, Walnut Creek, CA 94596

EXECUTIVE SUMMARY: In an acute oral toxicity study, five young adult, Hsd: Sprague Dawley SD rats/sex (Age: males - 8 weeks; females - 8 weeks; Weight: 214-238 g males; 175-185 g females; Source: Harlan Sprague Dawley, Inc.) were given a single oral dose of V-1283 72 WDG (72.1% Etoxazole; Lot No. VDL-563-45; Valent Lot No. VKB-100DG-3; brown granules) at 5000 mg/kg. The test material was ground and then prepared as a 75% w/v preparation during the dosing period. Body weights were obtained prior to fasting on day -1, prior to dosing on day 0 and on days 7 and 14. Animals were observed for clinical signs of toxicity and mortality for 14 days post dosing. A gross necropsy examination was performed on all animals at scheduled euthanasia.

Oral LD_{50} Males => 5000 mg/kg (observed); Oral LD_{50} Females => 5000 mg/kg (observed)

V-1283 72 WDG is classified as Toxicity Category IV based on the observed LD_{50} value in males and females.

All animals survived and gained weight during the study. Clinical signs included breathing abnormalities (congested breathing and rales), soft/mucoid stools, fecal staining, and dark material around the facial area. Two incidences of foci present on the thymus (left/both lobes) in two males. No gross abnormalities were noted at necropsy in females.

This study is classified as Acceptable (870.1100) and satisfies the guideline requirement for an acute oral study in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

RESULTS:

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Combined
5000	0/5	0/5	0/10

OBSERVATIONS: All animals survived and gained weight during the study. Clinical signs included breathing abnormalities (congested breathing and rales), soft/mucoid stools, fecal staining, and dark material around the facial area.

GROSS NECROPSY: Two incidences of foci present on the thymus (left/both lobes) in two male animals. No gross abnormalities were noted at necropsy in females.

DATA EVALUATION RECORD

STUDY TYPE: ACUTE DERMAL TOXICITY TESTING (870.1200 formerly §81-2)

Product Manager: 04 **Reviewer:** Rick J. Whiting

TEST MATERIAL PURITY: V-1283 72 WDG; 72% Etoxazole

CITATION: Rodabaugh, D. (2001) An acute dermal toxicity in rats with V-1283 72 WDG. Springborn Laboratories, Inc., Spencerville, Ohio. Laboratory Report Number 3548.16. November 16, 2001. MRID 45621618. Unpublished.

SPONSOR: Valent U.S.A. Corporation, 1333 N. California Blvd., Suite 600, Walnut Creek, CA 94596

EXECUTIVE SUMMARY: In an acute dermal toxicity study, five adult Hsd: Sprague Dawley SD rats/sex (Age: males - 9-10 weeks; females - 10 weeks; Weight: 290-342 g males; 208-222 g females; Source: Harlan Sprague Dawley, Inc.) were dermally exposed to a single application of V-1283 72 WDG (72.1% Etoxazole; Lot No. VDL-563-45; Valent Lot No. VKB-100DG-3; brown granules) at 5000 mg/kg (limit dose) for 24 hours. The test material was ground and then moistened with deionized water to form a paste which was applied to approximately 10% of the body surface area. Animals were observed for dermal irritation, clinical signs of toxicity and mortality daily for 14 days. A gross necropsy examination was performed on all animals at the time of scheduled euthanasia.

Dermal LD_{50} Males => 5000 mg/kg (observed); Dermal LD_{50} Females => 5000 mg/kg (observed)

V-1283 72 WDG is classified as Toxicity Category IV based on the observed LD_{50} value in both sexes.

One male was found dead on day 7. Necropsy results of this animal indicated a hernia on the diaphragm. The death was not considered to be treatment-related. A slight body weight loss was observed in two females during the study day 0 to 7. All other animals gained weight. All animals exceeded their initial body weight by the of the study (day 14). Clinical signs noted were dark material around the nose, eyes and/or mouth. Dermal irritation was noted at all test sites. No gross abnormalities were noted at necropsy on study day 14.

This study is classified as Acceptable (870.1200) and satisfies the guideline requirement for an acute dermal study in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

RESULTS:

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Combined
5000	1/5	0/5	1/10

OBSERVATIONS: One male was found dead on day 7. Necropsy results of this animal indicated a hernia on the diaphragm. The death was not considered to be treatment-related. A slight body weight loss was observed in two females during the study day 0 to 7. All other animals gained weight. All animals exceeded their initial body weight by the of the study (day 14). Clinical signs noted were dark material around the nose, eyes and/or mouth. Dermal irritation was noted at all test sites. No gross abnormalities were noted at necropsy on study day 14.

GROSS NECROPSY: No gross abnormalities were noted at necropsy.

DATA EVALUATION RECORD

STUDY TYPE: ACUTE INHALATION TOXICITY TESTING (870.1300 formerly §81-3)

Product Manager: 04 **Reviewer:** Rick J. Whiting

TEST MATERIAL PURITY: V-1283 72 WDG; 72% Etoxazole

CITATION: Rodabaugh, D. (2001) An acute nose-only inhalation toxicity in rats with V-1283 72 WDG. Springborn Laboratories, Inc., Spencerville, Ohio. Laboratory Report Number 3548.17. November 20, 2001. MRID 45621619 Unpublished.

SPONSOR: Valent U.S.A. Corporation, 1333 N. California Blvd., Suite 600, Walnut Creek, CA 94596

EXECUTIVE SUMMARY: In an acute inhalation toxicity study, five young adult Hsd: Sprague-Dawley SD rats/sex (Age: approximately 11 weeks; Weight: 305-359 g males; 210-230 g females; Source: Harlan Sprague-Dawley, Inc., Indianapolis, IN) were exposed by nose only inhalation to V-1283 72 WDG (72.1% Etoxazole; Lot No. VDL-563-45; Valent Lot No. VKB-100DG-3; brown granules) at 2.28 mg/L for four hours. Body weights were obtained prior to dosing on day 0 and on days 7 and 14.

All animals were observed for clinical signs of toxicity and mortality during the exposure, and for approximately 30 minutes and 1 hour after exposure on day 0 (post-exposure) and daily thereafter (days 1-14). A gross necropsy examination was performed on all animals at the scheduled euthanasia.

Inhalation LC_{50} Males => 2.28 mg/L (observed); Inhalation LC_{50} Females = > 2.28 mg/L (observed)

V-1283 72 WDG is classified as Toxicity Category IV based on the observed LC_{50} values in both sexes.

All animals survived the study. A slight body weight loss was noted for three males and three females during the study day 0 to 7 body weight interval and for two females during the study day 7 to 14 body weight interval. By study termination all animals had exceeded or maintained their initial body weight. Clinical observations included congested breathing and dark material around the eyes, nose or mouth. The animals recovered from these symptoms by day 1. The gravimetric chamber concentration was 2.28 mg/L. The mass median aerodynamic diameter was estimated to be 3.4 μm with a geometric standard deviation of 1.96. No significant gross abnormalities were noted at necropsy.

This study is classified as Acceptable (870.1300) and satisfies the guideline requirement for an acute inhalation study in the rat.

DATA EVALUATION RECORD

STUDY TYPE: PRIMARY EYE IRRITATION TESTING (870.2400 formerly §81-4)

Product Manager: 04 **Reviewer:** Rick J. Whiting

TEST MATERIAL PURITY: V-1283 72 WDG; 72% Etoxazole

CITATION: Rodabaugh, D. (2001) A primary eye irritation in rabbits with V-1283 72 WDG. Springborn Laboratories, Inc., Spencerville, Ohio. Laboratory Report Number 3548.18. November 16, 2001. MRID 45621620. Unpublished.

SPONSOR: Valent U.S.A. Corporation, 1333 N. California Blvd. , Suite 600, Walnut Creek, CA 94596

EXECUTIVE SUMMARY: In a primary eye irritation study, 0.0570 g (0.1 mL weight equivalent) of V-1283 72 WDG (72.1% Etoxazole; Lot No. VDL-563-45; Valent Lot No. VKB-100DG-3; brown granules) was placed into the conjunctival sac of the right eye of three adult New Zealand White rabbits (1 male and 2 female; Source: Myrtle's Rabbitry, Thompson Station, TN). All animals were observed for ocular irritation at 1, 24, 48 and 72 hours and up to 7 days post-instillation.

V-1283 72 WDG is classified as Toxicity Category III based on the moderate irritation observed and resolution by day 7.

Corneal opacity was observed in 3/3 eyes at the 24-hour scoring interval. The corneal opacity was resolved in all test eyes by the 72-hour scoring interval. Iritis was observed in 3/3 eyes at the 1-hour scoring interval and was completely resolved in all eyes by the 48-hour scoring interval. Conjunctivitis (redness - 3/3, swelling - 3/3 and discharge - 1/3) was noted in test eyes at the 1-hour scoring interval. The conjunctival irritation was completely resolved in all eyes by day 7.

This study is classified as Acceptable (870.2400) and satisfies the guideline requirement for a primary eye irritation study in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

RESULTS:

Observations	Number "positive"/number tested				
	Hours				Days
	1	24	48	72	7
Corneal Opacity	0/3	3/3	2/3	0/3	0/3
Iritis	3/3	1/3	0/3	0/3	0/3
Conjunctivae:					
Redness*	3/3	3/3	1/3	1/3	0/3
Chemosis*	3/3	1/3	1/3	0/3	0/3
Discharge*	1/3	0/3	0/3	0/3	0/3

*Score of 2 or more required to be considered "positive."

OBSERVATIONS: Corneal opacity was observed in 3/3 eyes at the 24-hour scoring interval. The corneal opacity was resolved in all test eyes by the 72-hour scoring interval. Iritis was observed in 3/3 eyes at the 1-hour scoring interval and was completely resolved in all eyes by the 48-hour scoring interval. Conjunctivitis (redness - 3/3, swelling - 3/3 and discharge - 1/3) was noted in test eyes at the 1-hour scoring interval. The conjunctival irritation was completely resolved in all eyes by day 7.

DATA EVALUATION RECORD

STUDY TYPE: PRIMARY DERMAL IRRITATION TESTING (870.2500 formerly §81-5)

Product Manager: 04 **Reviewer:** Rick J. Whiting

TEST MATERIAL PURITY: V-1283 72 WDG; 72% Etoxazole

CITATION: Rodabaugh, D. (2001) A primary skin irritation in rabbits with V-1283 72 WDG. Springborn Laboratories, Inc., Spencerville, Ohio. Laboratory Report Number 3548.19. November 19, 2001. MRID 45621621. Unpublished.

SPONSOR: Valent U.S.A. Corporation, 1333 N. California Blvd. , Suite 600, Walnut Creek, CA 94596

EXECUTIVE SUMMARY: In a primary skin irritation study, three adult male New Zealand White rabbits (Age: approximately 20 weeks; Source: Myrtle's Rabbitry, Thompson Station, TN) were dermally exposed to 0.5 g of V-1283 72 WDG (72.1% Etoxazole; Lot No. VDL-563-45; Valent Lot No. VKB-100DG-3; brown granules) as a single dermal application for 4 hours. The test material was moistened with deionized water and applied to a single 1 inch x 1 inch intact dose site on each animal. Animals were examined for signs of erythema and edema and the responses scored at 1hour after patch removal and 24, 48 and 72 hours after patch removal.

V-1283 72 WDG is classified as Toxicity Category IV based on the observations in this study.

Primary Dermal Irritation Index (PDII) = 1.58 Very slight to well defined erythema and very slight edema to slight were observed on 3/3 test sites at the 1-hour scoring interval. All sites were free of dermal irritation by the 72-hour scoring interval.

This study is classified as Acceptable (870.2500) and satisfies the guideline requirement for a primary skin irritation study in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

RESULTS: Primary Dermal Irritation Index (PDII) = 1.58

OBSERVATIONS: Very slight to well defined erythema and very slight edema were observed on 3/3 test sites at the 1-hour scoring interval. All sites were free of dermal irritation by the 72-hour scoring interval.

DATA EVALUATION RECORD

STUDY TYPE: DERMAL SENSITIZATION TESTING (870.2600 formerly §81-6)

Product Manager: 04 **Reviewer:** Rick J. Whiting

TEST MATERIAL PURITY: V-1283 72 WDG; 72% Etoxazole

CITATION: Rodabaugh, D. (2001) A dermal sensitization in guinea pigs with V-1283 72 WDG - Modified Buehler Design. Springborn Laboratories, Inc., Spencerville, Ohio. Laboratory Report Number 3548.20. November 15, 2001. MRID 45621622. Unpublished.

SPONSOR: Valent U.S.A. Corporation, 1333 N. California Blvd. , Suite 600, Walnut Creek, CA 94596

EXECUTIVE SUMMARY: In a dermal sensitization study conducted with V-1283 72 WDG (72.1% Etoxazole; Lot No. VDL-563-45; Valent Lot No. VKB-100DG-3; brown granules), 30 young adult male and female Hartley-derived albino guinea pigs (Age: males - 7 weeks; females - 8 weeks; Source: Hilltop Lab Animals, Inc., Scottdale, PA) were tested using a modified Buehler design. Preliminary testing was conducted to determine the correct concentrations for induction and challenge. Twenty test animals were induced with three applications (six hours/exposure, once per week for three weeks) of 0.30 g of test material at 100% concentration (moistened with 3 drops of deionized water). On day 27, 0.3 g of test material at 100% concentration (moistened with 3 drops of deionized water) was applied to the twenty test guinea pigs and to ten naive control guinea pigs for a six-hour challenge exposure. Test sites were graded for irritation at 24 and 48 hours after each induction and after the challenge. A positive control study using α-hexylcinnamaldehyde (HCA) was conducted within six months of the main study to validate the test system.

V-1283 72 WDG is classified as a non-sensitizer based on the results of this study.

Slight patchy erythema to moderate erythema was noted on all test animals during the induction phase. Very slight edema to slight edema was also observed at 10/20 test sites during the induction phase. Following the challenge, dermal reactions in the test and challenge control animals were limited to scores of "no reaction" to "slight patchy erythema." Group mean dermal scores were similar in the test animals as compared with the challenge control animals. Based on these results, the test substance is not considered to be a contact sensitizer. The positive response observed in the HCA study validates the test system used in this study.

This study is classified as Acceptable (870.2600) and satisfies the guideline requirement for an dermal sensitization study in the guinea pig.

COMPLIANCE: Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

PROCEDURE: In a dermal sensitization study conducted with V-1283 72 WDG (72.1% Etoxazole; Lot No. VDL-563-45; Valent Lot No. VKB-100DG-3; brown granules), 30 young adult male and female Hartley-derived albino guinea pigs (Age: males - 7 weeks; females - 8 weeks; Source: Hilltop Lab Animals, Inc., Scottdale, PA) were tested using a modified Buehler design. Preliminary testing was conducted to determine the correct concentrations for induction and challenge. Twenty test animals were induced with three applications (six hours/exposure, once per week for three weeks) of 0.30 g of test material at 100% concentration (moistened with 3 drops of deionized water). On day 27, 0.3 g of test material at 100% concentration (moistened with 3 drops of deionized water) was applied to the twenty test guinea pigs and to ten naive control guinea pigs for a six-hour challenge exposure. Test sites were graded for irritation at 24 and 48 hours after each induction and after the challenge. A positive control study using α-hexylcinnamaldehyde (HCA) was conducted within six months of the main study to validate the test system.

RESULTS: Slight patchy erythema to moderate erythema was noted on all test animals during the induction phase. Very slight edema to slight edema was also observed at 10/20 test sites during the induction phase. Following the challenge, dermal reactions in the test and challenge control animals were limited to scores of "no reaction" to "slight patchy erythema." Group mean dermal scores were similar in the test animals as compared with the challenge control animals. Based on these results, the test substance is not considered to be a contact sensitizer. The positive response observed in the HCA study validates the test system used in this study.

ACUTE TOX ONE-LINERS

1. **DP BARCODE:** D283724
2. **PC CODE:** 107091
3. **CURRENT DATE:** 05/SEPT/2002
4. **TEST MATERIAL:** V-1283 72 WDG (72% Etoxazole; Lot No. VDL-563-45; Valent Lot No. VKB-100DG-3; brown granules)

Study/Species/Lab Study # /Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity/rat Springborn Laboratories, Inc. 3548.15 / 08-13-01	45621617	LD_{50} => 5000 mg/kg (males and females)	IV	A
Acute dermal toxicity/rat Springborn Laboratories, Inc. 3548.16 / 11-16-01	45621618	LD_{50} => 5000 mg/kg (males and females)	IV	A
Acute inhalation toxicity/rat Springborn Laboratories, Inc. 3548.17 / 11-20-01	45621619	LC_{50} => 2.28 mg/L (males and females)	IV	A
Primary eye irritation/rabbit Springborn Laboratories, Inc. 3548.18 / 11-16-01	45621620	Moderate irritant	III	A
Primary dermal irritation/rabbit Springborn Laboratories, Inc. 3548.19 / 11-19-01	45621621	Slight irritant	IV	A
Dermal sensitization/guinea pig Springborn Laboratories, Inc. 3548.20 / 11-15-01	45621622	Non-sensitizer	–	A

Core Grade Key: **A =Acceptable, S = Supplementary, U = Unacceptable, V = Self Validated**

COMPLIANCE: Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

RESULTS:

Exposure Concentration mg/L (Gravimetrically Determined)	Number of Deaths/Number Tested		
	Males	Females	Combined
2.28	0/5	0/5	0/10

Chamber Atmosphere		
Gravimetric conc.	MMAD	GSD
2.28 mg/L	3.4 µm	±1.96

Chamber Environment[a]	
Chamber Volume	10 L
Airflow	35 LPM
Temperature	74.4-77.2 ^{0}F
Relative Humidity	44.2-48.4%

[a] Nose only

OBSERVATIONS: All animals survived the study. A slight body weight loss was noted for three males and three females during the study day 0 to 7 body weight interval and for two females during the study day 7 to 14 body weight interval. By study termination all animals had exceeded or maintained their initial body weight. Clinical observations included congested breathing and dark material around the eyes, nose or mouth. The animals recovered from these symptoms by day 1.

GROSS NECROPSY: No significant gross abnormalities were noted at necropsy.